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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,950	12/30/2004	Rainer Hipfel	P67772US1	3111

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EXAMINER	
CHERNYSHEV, OLGA N	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 08/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/509,950	HIPFEL ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *11,12 and 21-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 October 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/15/4*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in the reply filed on June 16, 2006 is acknowledged.

Claims 11-12 and 21-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on June 16, 2006.

Claims 1-10 and 13-20 are under examination in the instant office action.

Sequence compliance

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821 (a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825. Specifically, no sequence identification has been provided for the nucleic acid sequences presented on pages 29-30 and in Figure 5 (mouse TARPP) of the instant specification. In case these sequences are new, Applicant needs to provide a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a substitute paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). The instant specification will also need to be amended so that it complies with 37

C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. See M.P.E.P. 2422.04.

3. The text of the instant specification, including claims, is not in compliance with the requirements for Sequence Identifiers (see MPEP 2422.03). The appropriate format for sequence identifiers is SEQ ID NO:X, wherein "X" is the sequence number. Appropriate correction is required.

Drawings

4. The figures of the instant application are presented on separate pages or in separate panels. 37 C.F.R. § 1.84(u) (1) states that in cases when figures present partial views of a drawing, which are intended to form one complete view, whether contained on one or several sheets, the figures must be identified by the same number followed by a capital letter. For example, the two pages of Figure 2 in the instant specification should be renumbered "Figure 2A" – "Figure 2B" rather than "Figure 2 a), b)". Applicant is reminded that once the drawings are changed to meet the separate numbering requirement of 37 C.F.R. § 1.84(u) (1), the specification should be amended to change the Brief Description of the Drawings and the rest of the specification to refer to each Figure accordingly. If, for example, Figure 2 is divided into Figures 2A-2B, then the Brief Description and all the references to this figure in the specification must refer to this Figure in the same manner.

Information Disclosure Statement

5. The information disclosure statement filed on November 15, 2004 fails to comply with 37 CFR 1.98(a)(2) and (b)(5), which require the following:

(a)(2) Any information disclosure statement filed under § 1.97 shall include [...] A legible copy of [each publication or that portion which caused it to be listed];

(b)(5) Each publication listed in an information disclosure statement must be identified by publisher, author (if any), title, relevant pages of the publication, date, and place of publication.

The information disclosure statement filed on November 15, 2004 has been considered in part. Specifically, reference AE has not been considered.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 8-10 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims fail to include any limitations which would distinguish the claimed proteins from those which occur in nature. In the absence of the hand of man, naturally occurring proteins are considered non-statutory subject matter. Diamond v. Chakrabarty, 206 USPQ 193 (1980). Filing of evidence of a new utility imparted by the increased purity of the claimed invention and amendment of the claims to recite a purity limitation, if supported by the

specification, is suggested to obviate this rejection. Applicant should point to the basis in the specification for any amendment to the claims.

8. Claims 1-10 and 13-20 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial credible asserted utility or a well-established utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect.

It is clear from the instant application that the protein described therein is what is termed an "orphan protein" in the art. The DNA of the instant application has been isolated because of its similarity to a known DNA. There is little doubt that, after complete characterization, this DNA and encoded protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is

insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a 'patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion".

The instant claims are drawn to an isolated nucleic acid molecule and the protein encoded thereby of as yet undetermined function or biological significance. It is clear from the instant specification that the claimed novel nucleic acid encodes "cAMP regulated phosphoprotein ARPP-21, herein designated as human TARPP (hTARPP)" (middle at page 5 of the instant specification). More specifically, "[t]he name "TARPP" was coined to reflect the thymocyte-specific protein expression in mice"; the disclosure presents data "of differential expression of hTARPP mRNA in post-mortem brains of patients suffering from Alzheimer's diseases in comparison to age-matched healthy individuals" (page 5). Thus, the instant human TARPP was isolated based on structural similarities to mouse homologous ARPP-21 splice variant protein, which was reported to accompany "T cell receptor gene arrangement and thymocyte education", to be expressed in murine brain; however, "[a] function for murine TARPP in the brain has not been described". With respect to analysis of protein structure, numerous publications exist on a topic of predicting protein functions from structural similarities or homology to the known proteins. It is well described in the art that amino acid structure cannot necessarily predict the function of the protein: "Knowing the protein structure by itself is insufficient to annotate a number of functional classes and is also insufficient for annotating the specific details of protein function" (see Skolnick et al., Box 2 on page 36 and the whole paper). Moreover, "Structural similarity does not necessarily mean a common evolutionary origin and homologous sequences may evolve into different folds (according to current classification schemes) (See Bork et al., Current Opinion in structural Biology, 1998, 8, page 332, first column, second paragraph). Thus,

according to the state of the art, functional characteristics of a protein cannot be unequivocally extrapolated from its structural characteristics. Moreover, in the instant case, in view of the current absence of knowledge of physiological relevance of the murine homologue of the instant disclosed hTARPP, no prediction of its function can be possibly made with respect to its similarity to the known murine homologue.

In the absence of knowledge of the biological significance of this specific nucleic acid and encoded protein, there is no immediately obvious patentable use for the polynucleotide or the encoded protein. According to the specification of the instant application "[t]o date, no experiments have been described that demonstrate a link between the dysregulation of ARPP-21 gene expression and neurodegenerative disorders. Particularly the disclosure in the present invention of the novel human TARPP (hTARPP) isoform, and the identification of a link of this isoform with neurodegenerative diseases, offers ways, inter alia, for the diagnosis and treatment of neurodegenerative disorders, in particularly Alzheimer's disease" (page 5 of the instant specification). However, the instant specification fails to provide any evidence or sound scientific reasoning that would support a conclusion that the instant nucleic acid or encoded protein is associated with any neurodegenerative diseases or disorder, including Alzheimer's diseases. The instant application also fails to demonstrate use of the protein or nucleic acid as a marker for any disease or condition (which would be a real world use). The limited information presented in Tables 1 and 2 appears to fail to disclose the critical level of frontal cortex/hippocampus ratio of the claimed TARPP molecules that is diagnostic of Alzheimer's disease.

Furthermore, because the instant specification does not teach a biological activity of the protein, which supports a practical utility, one would not reasonably believe that the evaluation of the level and/or activity of the claimed peptide would provide meaningful information about a condition or disease, like a neurodegenerative disease recited in claims 15-19. Also, because there is no information disclosed pertaining to the level of a transcription product or a translation product of the gene coding for hTARPP, which is clearly associated with a neurodegenerative condition, one skilled in the art would have to resort to a significant amount of further research in order to practice the methods as claimed in claims 13-14, for example. To employ a protein or an encoding nucleic acid of the instant invention in any of the disclosed methods would clearly be using it as the object of further research, which has been determined by the courts to be a utility, which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for the encoded protein in their currently available form, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-10 and 13-20 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a clear asserted utility or a

well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

9. Claims 9-10 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 9-10 are directed to protein molecules, which are fragments, derivatives or variants of a protein of SEQ ID NO: 1. The claims do not require that the polypeptide possess any particular conserved structure or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity. However, the instant specification fails to describe the entire genus of proteins, which are encompassed by these claims. In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of a nucleic acid molecule which encodes a protein which has the amino acid sequence of SEQ ID NO: 1. The claims are drawn to proteins, which are fragments, derivatives or variants of a protein of SEQ ID NO: 1. Thus, the claims are not limited to a protein with a specific amino acid sequence. The claims only require the claimed polypeptides to share some degree of structural similarity to the isolated protein of SEQ ID NO: 1. The specification only describes a protein having the amino acid sequence of SEQ ID NO: 1 and fails to teach or describe any other protein which lacks the amino acid sequence of SEQ ID NO: 1 and has the activities possessed by the hTARPP of the instant invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of "a fragment, derivative or variant of a protein of SEQ ID NO: 1". There is not even identification of any particular portion of the structure that must be conserved. As stated above, it is not even clear what region of the encoded polypeptide has the disclosed activity. The specification does not provide a complete structure of those proteins, which are fragments, derivatives or variants of a protein of SEQ ID NO: 1 and fails to provide a representative number of species for the claimed genus. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of

the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 1, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 4 and 13-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claim 4 is indefinite and ambiguous for recitation of hybridization "under stringent conditions". Without providing a precise set of hybridization conditions, in the claim or the specification, the metes and bounds of the claimed isolated nucleic acid molecule cannot be

defined. Also, recitation "capable of" renders the claim language indefinite because it is not clear whether this limitation is part of the invention. Clarification is required.

13. Claims 13-19 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the final step that leads to diagnosis, prognosis, determination of progression and evaluating a treatment. Claims 13-19, as written, do not contain a recitation of the step that allows achieving the goal stated in the claim preamble. Moreover, with respect to claim 19, since no clear association between "a level and/or activity" of hTARPP and a neurodegenerative diseases is currently disclosed, it is not clear and cannot be determined what alteration in that level and/or activity would mean to a skilled practitioner with respect to evaluating a treatment of a neurodegenerative disease.

Art of record

14. US Publication No.: US 2003/0186249, published October 02, 2003, filed April 01, 2002. The document discloses polypeptide and polynucleotide sequences, "human TARPP genes", which have 100% structural similarity to the instant claimed molecules.

Double Patenting

15. Applicant is advised that should claim 9 be found allowable, claim 10 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a

substantial duplicate of the allowed claim. See MPEP § 706.03(k). In the instant case, claims 9 and 10 recite "for use as ...". Because it appears that this recitation does not affect the structure of the claimed compound, the scope of the claimed subject matter of claims 9-10, which is limited to the protein of SEQ ID NO: 1, its fragments, derivatives and variants, is the same, as currently claimed.

Conclusion

16. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Art Unit 1649

August 8, 2006